

04-04-00

PATENT

A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



Applicant: Maury Zivitz
Serial No.: To Be Assigned
Filed: Herewith
For: BIOSENSOR
ELECTROMAGNETIC
NOISE CANCELLATION

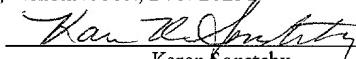
Docket No. 53009-223482

JC564 U.S. PTO
09/03/00
04/03/00

Box Patent Application
Assistant Commissioner for Patents
Washington, D.C. 20231

EXPRESS MAIL LABEL NO. EL210856535US

I CERTIFY THAT, ON APRIL 3, 2000, THIS PAPER IS BEING DEPOSITED
WITH THE UNITED STATES POSTAL SERVICE AS EXPRESS MAIL POST
OFFICE TO ADDRESSEE SERVICE UNDER 37 C.F.R. 1.10 IN AN
ENVELOPE ADDRESSED TO THE ASSISTANT COMMISSIONER FOR
PATENTS, WASHINGTON, D.C. 20231


Karen Sonsteb

TRANSMITTAL LETTER

Enclosed for filing are the following papers in connection with the above-identified
patent application:

1. New patent application consisting of: 7 Pgs. Specification, 23 Claims, 1 Pg. Abstract,
5 Sheets Informal Drawings;
2. Combined Declaration and Power of Attorney;
3. Assignment with Recordation Form Cover Sheet attached;
4. Check No. 489247 in the amount of \$ 784.00 to cover the filing fee and assignment
recordation fee;
5. Postcard.

A self-addressed return postcard in accordance with M.P.E.P. Section 503
itemizing all of the above-referenced documents filed with the United States
Patent and Trademark Office.

U.S. PATENT AND TRADEMARK OFFICE

In the event the amount submitted herewith is insufficient in any respect, the Commissioner is hereby authorized to charge the balance needed to our Deposit Account No. 06-0029 and notify us of the same.

Respectfully Submitted,

MAURY ZIVITZ

By:


John M. Haurykiewicz, #29,311
FAEGRE & BENSON LLP
2200 Norwest Center
90 South Seventh Street
Minneapolis, MN 55402-3901
612/336-3328

Dated: April 3, 2000

M2.20304639.01

BIOSENSOR ELECTROMAGNETIC NOISE CANCELLATION

Background of the Invention

In the past, it has been found desirable to use amperometric analysis of biosensing cell assemblies. Such analysis was possibly subject to electromagnetic interference because of the loop formed by such cells in their disposable form, wherein a pair of conductors were supported on an insulating substrate with a remote test cell completing the circuit for analysis of a response current, which in one embodiment may be a Cottrell current. In the prior art, any stray electromagnetic fields present to the biosensing cell assembly may cause a spurious signal ("noise"), interfering with and distorting the response current. The present invention overcomes this difficulty by providing a noise cancellation apparatus and method to improve the measurement of the response current in such biosensing cell assemblies.

Brief Description of the Drawings

Figure 1 is a prior art biosensing cell assembly.

Figure 2 is a biosensing cell assembly according to the present invention.

Figure 3 is a circuit diagram of a simplified circuit useful for energizing and measuring the response current in the biosensing cell assembly of Figure 2.

Figure 4 is a simplified block diagram of the biosensing cell assembly of Figure 2 and the circuit of Figure 3.

Figure 5 is a second embodiment of a biosensing cell assembly according to the present invention.

Figure 6 is a section view along line 6-6 of Figure 5.

Figure 7 is a still further embodiment of a biosensing cell assembly shown inserted into an instrument housing for energizing and reading the cell assembly according to the present invention.

Figure 8 is a view similar to that of Figure 7, but with the biosensing cell assembly removed from the instrument housing and showing further aspects of this embodiment of the present invention.

Figure 9 is a simplified electrical schematic of another form of a circuit useful for energizing and measuring the response current in the biosensing cell assembly according to the present invention.

Detailed Description of the Invention

Referring now to the figures, and most particularly to Figure 1, a prior art biosensor cell assembly 10 includes a pair of electrodes or conductors 12 and 14 which are supported on a polymeric sheet or substrate 16. A cover sheet 18 is provided with openings 20 and 24 which expose the conductors 12 and 14. Opening 20 creates a well and provides access to a reaction zone 22 between conductors 12 and 14. A gel-like layer (not shown) or other form of reactants overlays conductors 12 and 14 to form reaction zone 22. In operation, an analyte-containing fluid sample is preferably placed on the reaction zone 22 to determine the concentration of analyte using amperometric analysis. The prior art assembly 10 may be subject to electromagnetic interference when undergoing amperometric analysis, more particularly, stray electromagnetic fields may pass through a measurement loop 26 formed by the conductors 12 and 14 and the reaction zone 22. It is to be understood that the measurement loop 26 will form a complete circuit when connected to an instrument (as will be described *infra*) to perform the amperometric analysis.

Referring now to Figure 2, a first embodiment of the biosensor cell assembly 30 of the present invention may be seen. In this embodiment, the measurement loop 26 is the same or similar to that shown in Figure 1. In addition, however, there is a noise cancellation loop 32 physically arranged to be exposed to substantially the same electromagnetic environment as the measurement loop 26. The

noise cancellation loop 32 includes a pair of spaced apart conductors 34, 36 and a predetermined impedance 38. Impedance 38 may be a resistor and is preferably within a range of the impedance of the reaction zone or test cell 22 when the test cell 22 is amperometrically monitoring a response current to provide an indication of the analyte concentration being measured. For example, if the test cell 22 varies between 20K ohms and 100K ohms for various analyte concentrations to be measured, impedance 38 is preferably selected to be between 20K ohms and 100K ohms, and most preferably about 60K ohms, for a range of amperometric response currents from 10 to 50 microamperes.

As may be seen in Figure 2, loop 32 closely surrounds loop 26, generally circumscribes the same area, and is in generally the same plane, so that any ambient electromagnetic field will affect or influence loops 26 and 32 substantially the same. More particularly, any error current induced in measurement loop 26 will be substantially the same as an error current induced in the noise cancellation loop 32. Since loop 32 has a known, fixed impedance, the error current may be removed from loop 26 by subtracting the error current in loop 32. It is to be understood that the error currents and error subtraction occur only when the assembly 30 is connected to an instrument for amperometric analysis.

The electrical circuit schematic 40 for such a connection is shown in Figure 3. In this circuit 40, test cell 22 is connected to an amplifier 42 and powered by a DC voltage source 44. Measurement loop 26 will thus have a response current flowing through conductors 12 and 14 in a counterclockwise direction 46. The noise cancellation loop 32, formed by conductors 34 and 36 and resistor 38 will have a current produced by source 44 flowing therethrough in a clockwise direction 48. Loop 32 may thus be seen to be arranged to be in an “anti-parallel” relationship with loop 26. Since a stray ambient electromagnetic field will induce substantially the same currents in each of loops 32 and 26 (i.e., the induced currents will be substantially the same in magnitude and in direction), the total currents in those loops may be added together at the negative summing junction 51 of amplifier 42, canceling or reducing the effect of the electromagnetic interference. It is to be understood that

the DC current through resistor 38 will be a fixed offset to the response current in loop 26 and can be accounted for in a conventional manner. Resistor 38 preferably has a “flat” frequency response, such that the impedance in the noise cancellation loop 32 is substantially frequency independent. It is to be understood, however, that there is an inductance associated with each of the loops 26 and 32, and that such inductances are preferably made as similar as possible, such that the total impedance of loop 32 has substantially the same frequency response as the total impedance of loop 26, taking into account the conductors, any stray capacitance, and the test cell 22 (for loop 26) or resistor 38 (for loop 32). The voltage source 44 and amplifier 42 provide the means for determining the response current to provide an indication of an analyte concentration in the test cell or reaction zone 22.

It is to be further understood that the amperometric response current measured by the circuit 40 of Figure 3 will have a modified characteristic from that when the prior art sensor 10 is used without the noise cancellation loop. More particularly, when the noise cancellation loop 32 is connected, the change in impedance of test cell 22 will be that of a variable resistor (depending upon analyte concentration) in parallel with a fixed resistor 38. The gain of circuit 40 will be the ratio of a feedback resistor 50 to the parallel equivalent of the impedances 22 and 38. Conventional offset and calibration subcircuits (not shown) may be used with amplifier 42 according to well-known techniques. It is to be understood that the output 52 of operational amplifier 42 is preferably further processed to provide signal conditioning by additional circuitry (also not shown). Such additional circuitry may include scaling, switching, and analog to digital conversion, as is well known for amperometric analysis of response currents, for example measurement and display of glucose concentration in the reaction zone 22 by measurement of Cottrell current.

Referring now to Figure 4, an alternative embodiment of the biosensing cell assembly 130 may be seen. In this embodiment, the measurement loop 26 and the noise cancellation loop 32 are positioned adjacent each other on a common substrate 116. Even though the same field lines will not pass through both loops, such an arrangement will expose both loops to substantially the same electromagnetic

environment, especially where field gradients are low, as is expected in the regions where amperometric analyses are expected to take place.

Referring now to Figures 5 and 6, a still further alternative embodiment of a biosensing cell assembly 230 may be seen. In this embodiment, the measurement loop 26 is located on one side of a substrate 216, while the noise measurement loop 32 is located on other side of substrate 216. In this embodiment, loops 26 and 32 are preferably substantially congruent to each other and separated only by the thickness of substrate 216.

Referring now to Figures 7 and 8, a still further alternative embodiment of the present invention may be seen. This embodiment makes use of the prior art biosensing cell assembly 10 and provides a shelf or support 54 carrying the noise cancellation loop 32. In operation, assembly 10 carrying conductors 12 and 14 and reaction zone 22 of the measurement loop 26 is inserted into a measuring instrument 56, as shown in Figure 7. As may be most clearly seen in comparison with Figure 8 (showing the noise cancellation loop 32 in shelf 54) the measurement loop 26 will be physically aligned with (and generally preferably substantially congruent to) the noise cancellation loop 32 when the test strip or assembly 10 is inserted into the instrument 56. Thus this embodiment has the instrument 56 electrically connectable to the measuring loop 26 and has the noise cancellation loop 32 located on the structure 54 adjacent the measurement loop 26 when the measurement loop is connected to the instrument.

Referring now to Figure 9, an alternative (simplified) schematic 340 for the biosensing cell assembly 330, power source 344 and amplifier 342 may be seen. In this embodiment it is to be understood that the response current caused by voltage source 344 flows in a counterclockwise direction 46 in the measurement loop 26. Similarly, current caused by voltage source 344 in the noise cancellation loop 32 flows in a counterclockwise direction, indicated by arrow 46. The noise cancellation loop 32 is connected to an inverting input 62 of an amplifier 64. An output 66 of amplifier 64 is connected through a summing resistor 70 to the inverting input 51 of amplifier 342. A feedback resistor 68 is connected between the inverting input 62

and the output 66 of amplifier 64. Feedback resistor 68 is preferably sized to set the gain of amplifier 66 in a conventional manner using the ratio of the resistance of resistor 68 to the resistance of resistor 38 (assuming the impedance of source 344 is negligible). Summing resistor 70 is preferably selected to make the steady state output of the noise cancellation loop 32 equal to that of measurement loop 26.

In the embodiment shown in Figure 9, it is to be understood that any stray electromagnetic field will cut both loops 26 and 32 substantially identically, and thus induce in-phase currents in each loop. By summing the output of the measurement loop 26 with an inverted signal (from amplifier 64) representing the output of the noise cancellation loop 32 at the inverting input 51 of amplifier 342, the error induced by a stray field in the electromagnetic environment may be effectively subtracted from the measurement loop signal. The resistance value of resistors 70 and 68 may be selected to optimize the error correction. By way of contrast, the phases of the electromagnetically induced signals or currents in the arrangement shown in Figures 2 and 3 are 180 degrees out of phase and thus need to be added to cancel.

Additionally, it is to be understood that when the effective impedances of loops 26 and 32 are unequal, the induced error currents will not cancel completely; however, in such circumstances, a reduction in error caused by induced currents from the electromagnetically propagated field energy irradiating the biosensor cell assembly will occur, even if the error is not eliminated entirely.

The present invention may thus be seen to include a method of reducing electromagnetic interference in a measurement loop of the type providing an indication of analyte concentration using a response current passing through a test cell by way of a pair of conductors on a substrate. In one form, the method includes physically aligning a noise cancellation loop with the measurement loop formed by the test cell and pair of conductors on a substrate, and connecting the noise cancellation loop in anti-parallel with the measurement loop such that any stray electromagnetic field induced current in the measurement loop is cancelled by a current induced by the same stray electromagnetic field in the noise cancellation loop.

The method may include forming the noise cancellation loop and the measurement loop on the same test strip. Alternatively, the method may include providing the measurement loop on a disposable test strip and providing the noise cancellation loop on an instrument such that the noise cancellation loop is physically aligned with the measurement loop when the test strip is connected to the instrument.

This invention is not to be taken as limited to all of the details thereof as modifications and variations thereof may be made without departing from the spirit or scope of the invention.

What is Claimed Is:

1. A biosensing cell assembly comprising:
 - a. a substrate having a proximal end and a distal end;
 - b. a measurement loop located on the substrate, the measurement loop including:
 - i. a pair of spaced-apart conductors each having a proximal end and a distal end, the proximal ends located at the proximal end of the substrate for connection to an instrument,
 - ii. a test cell connected across the distal ends of the conductors, the test cell having an analyte reaction zone with an electrical impedance that varies in response to analyte concentration; and
 - c. a noise cancellation loop physically arranged to be exposed to substantially the same electromagnetic environment as the measurement loop and electrically connected to substantially cancel the effect of electromagnetically propagated field energy irradiating the biosensor cell assembly.
2. The biosensing cell assembly of claim 1 wherein the noise cancellation loop is on the substrate.
3. The biosensing cell assembly of claim 2 wherein the measurement loop and the noise cancellation loop are on the same side of the substrate.
4. The biosensing cell assembly of claim 3 wherein the measurement loop and the noise cancellation loop circumscribe generally the same area.
5. The biosensing cell assembly of claim 3 wherein the measurement loop and the noise cancellation loop are located adjacent each other.

6. The biosensing cell assembly of claim 2 wherein the measurement loop and the noise cancellation loop are on opposite sides of the substrate.
7. The biosensing cell assembly of claim 6 wherein the measurement loop and the noise cancellation loop are substantially congruent.
8. The biosensing cell assembly of claim 1, further comprising an instrument electrically connectable to the measurement loop, and further wherein the noise cancellation loop is located on a structure adjacent the measurement loop when the measurement loop is connected to the instrument.
9. The biosensing cell assembly of claim 8 wherein the noise cancellation loop is substantially congruent to the measurement loop.
10. The biosensing cell assembly of claim 1 wherein the measurement loop is physically arranged to have a first current induced therein having a first phase associated therewith when exposed to an ambient electromagnetic field and wherein the noise cancellation loop is physically arranged to have a second current induced therein, the second current having a second phase associated therewith when the noise cancellation loop is exposed to the same ambient electromagnetic field and wherein the first and second currents are combined to substantially reduce the effect of the ambient electromagnetic field on the biosensing cell assembly.
11. The biosensing cell of claim 10 wherein the first and second currents are combined to substantially cancel the effect of the ambient electromagnetic field on the biosensing cell assembly.

- PCT/US2016/032006
12. The biosensing cell assembly of claim 10 further including means for determining a response current to provide an indication of an analyte concentration.
 13. The biosensing cell assembly of claim 12 wherein the means for determining the response current comprises a voltage source to apply a voltage across the test cell via the pair of conductors in the measurement loop and an amplifier connected to amplify the response current resulting therefrom.
 14. The biosensing cell assembly of claim 13 wherein the measurement loop and the noise cancellation loop are physically arranged to have the phase of the second current displaced by 180 degrees from the phase of the first current and the measurement loop and the noise cancellation loop are electrically connected to add the first and second currents together.
 15. The biosensing cell assembly of claim 13 wherein the measurement loop and the noise cancellation loop are physically arranged to have the first and second currents in phase with each other and the measurement loop and the noise cancellation loop are electrically connected to subtract the second current from the first current.
 16. The biosensing cell assembly of claim 1 wherein the electrical impedance of the test cell varies within a predetermined range in response to various concentrations of the analyte.
 17. The biosensing cell assembly of claim 16 wherein a predetermined impedance is included in the noise cancellation loop.
 18. The biosensing cell assembly of claim 17 wherein the predetermined impedance included in the noise cancellation loop is within the impedance

range of the test cell when the test cell is amperometrically monitoring a response current to provide an indication of the analyte concentration.

19. The biosensing cell assembly of claim 17 wherein the impedance in the noise cancellation loop is substantially frequency independent.
20. The biosensing cell assembly of claim 17 wherein the noise cancellation loop has a pair of conductors, and the combination of the impedance in the noise cancellation loop, together with the conductors of the noise cancellation loop, has substantially the same frequency response characteristics as the combination of the test cell and conductors of the measurement loop.
21. A method of reducing electromagnetic interference in a measurement loop of the type providing an indication of analyte concentration using a response current passing through a test cell by way of a pair of conductors on a substrate, the method comprising:
 - a. physically aligning a noise cancellation loop with a measurement loop formed by the test cell and pair of conductors on a substrate; and
 - b. connecting the noise cancellation loop in anti-parallel with the measurement loopsuch that any stray electromagnetic field induced current in the measurement loop is cancelled by a current induced by the same stray electromagnetic field in the noise cancellation loop.
22. The method of claim 21 wherein step a further comprises forming the noise cancellation loop and the measurement loop on the same test strip.
23. The method of claim 22 wherein step a further comprises providing the measurement loop on a disposable test strip and providing the noise cancellation loop on an instrument such that the noise cancellation loop is

physically aligned with the measurement loop when the test strip is connected to the instrument.

Abstract

A biosensing cell assembly having a measurement loop with a test cell having an analyte reaction zone for amperometric measurement of a response current to determine analyte concentration and a noise cancellation loop arranged to be physically exposed to the same electromagnetic environment as the measurement loop. The noise cancellation loop has a predetermined impedance within a range of the impedance of the test cell analyte reaction zone and provides a current to cancel or reduce the effects of the electromagnetic environment on the measurement loop.

M2:20281805.04

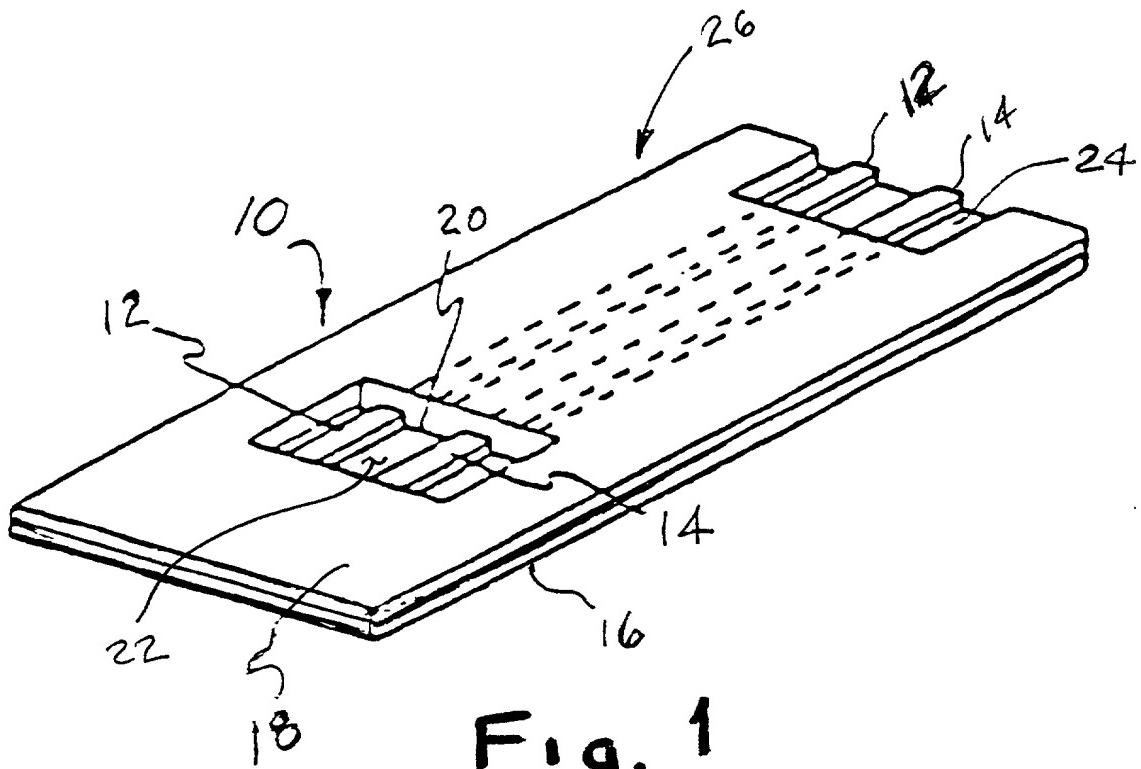


Fig. 1
PRIOR ART

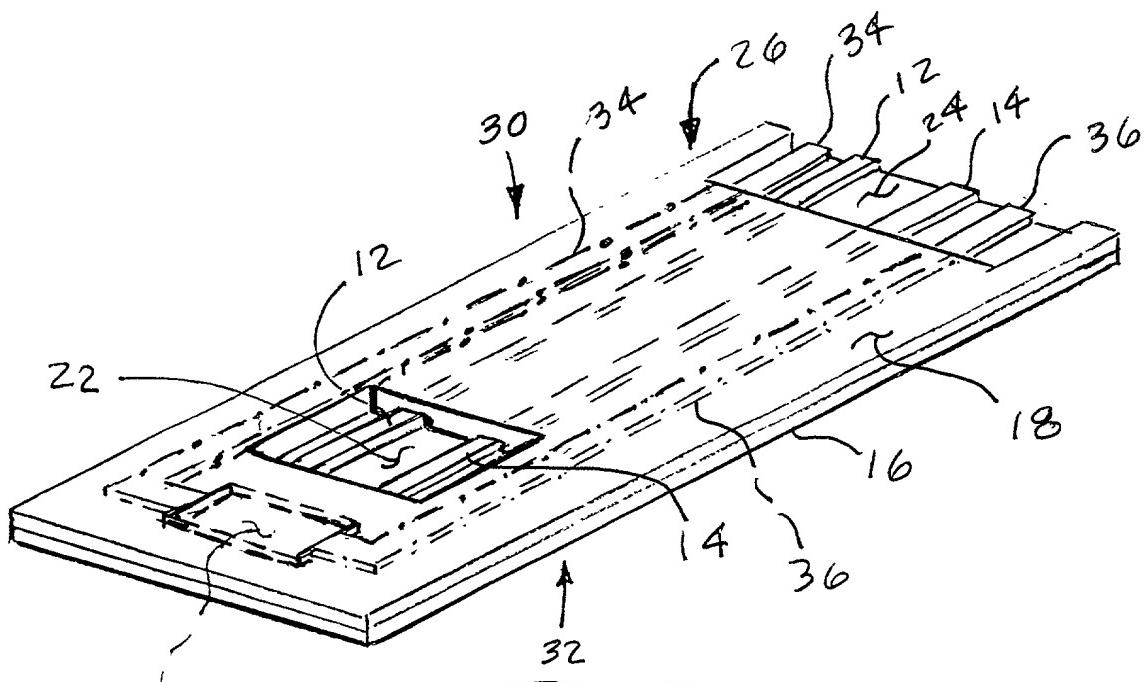


Fig 2

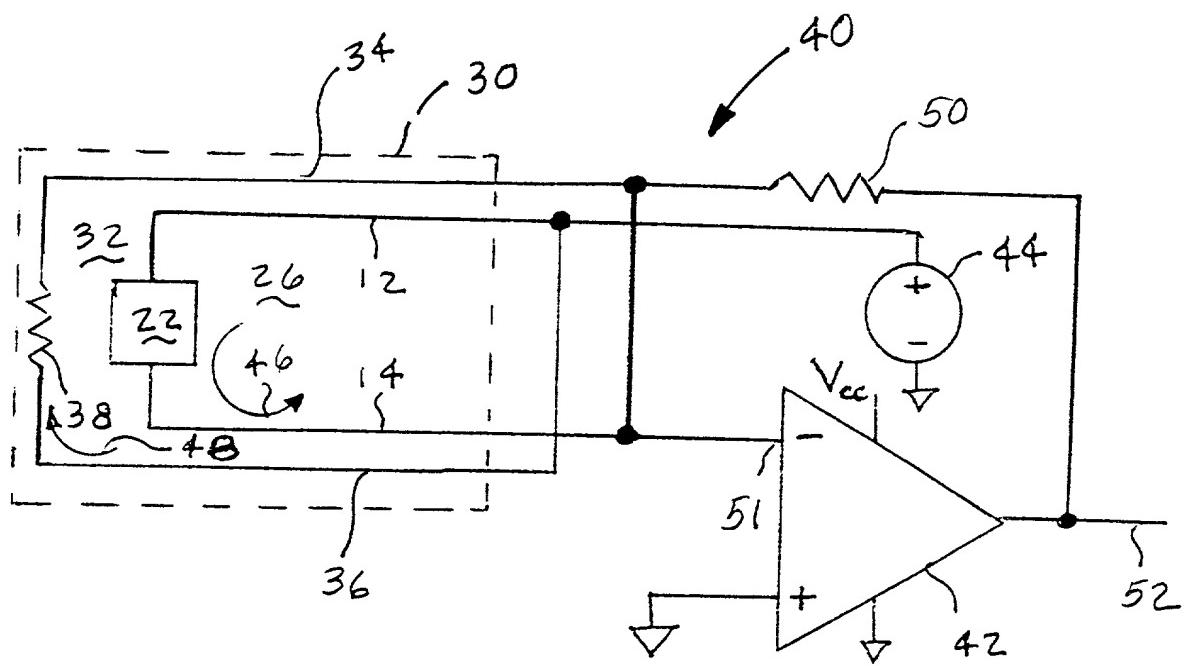
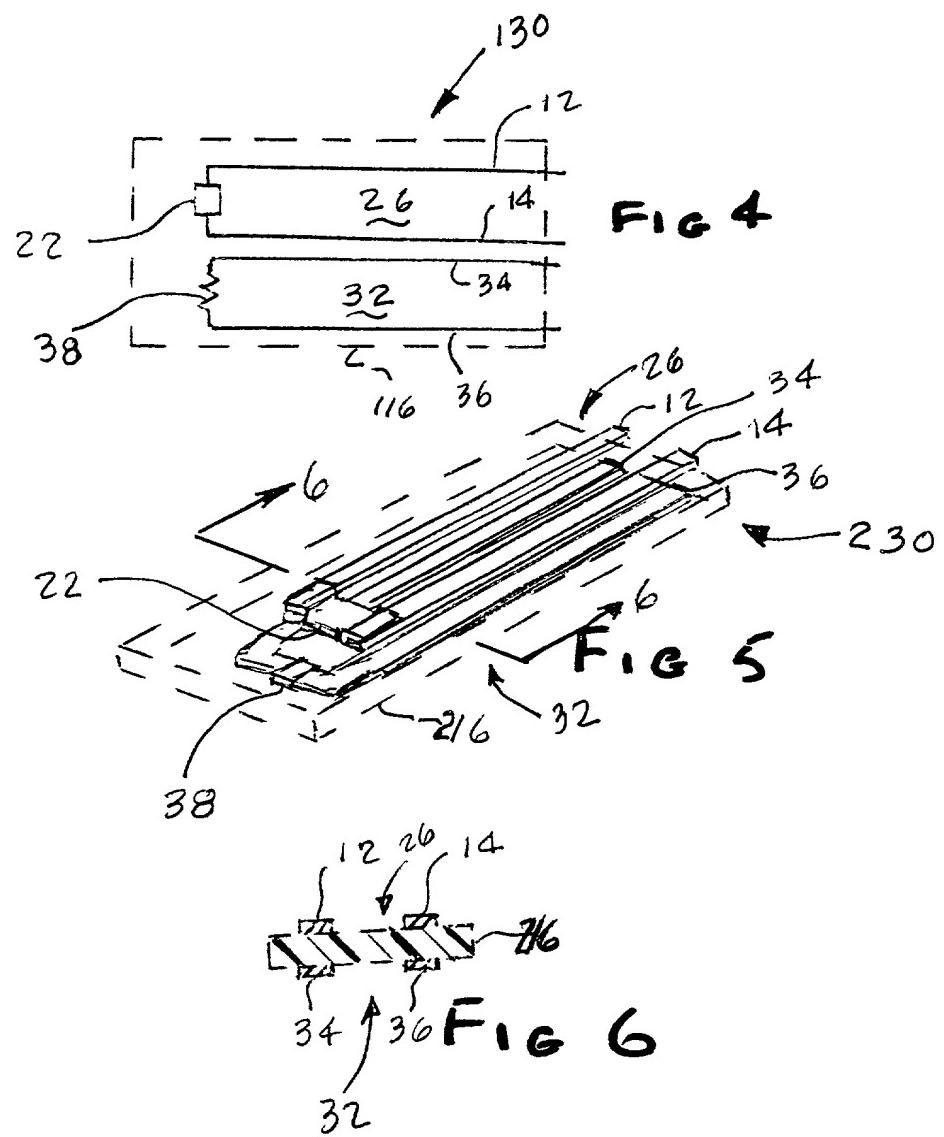
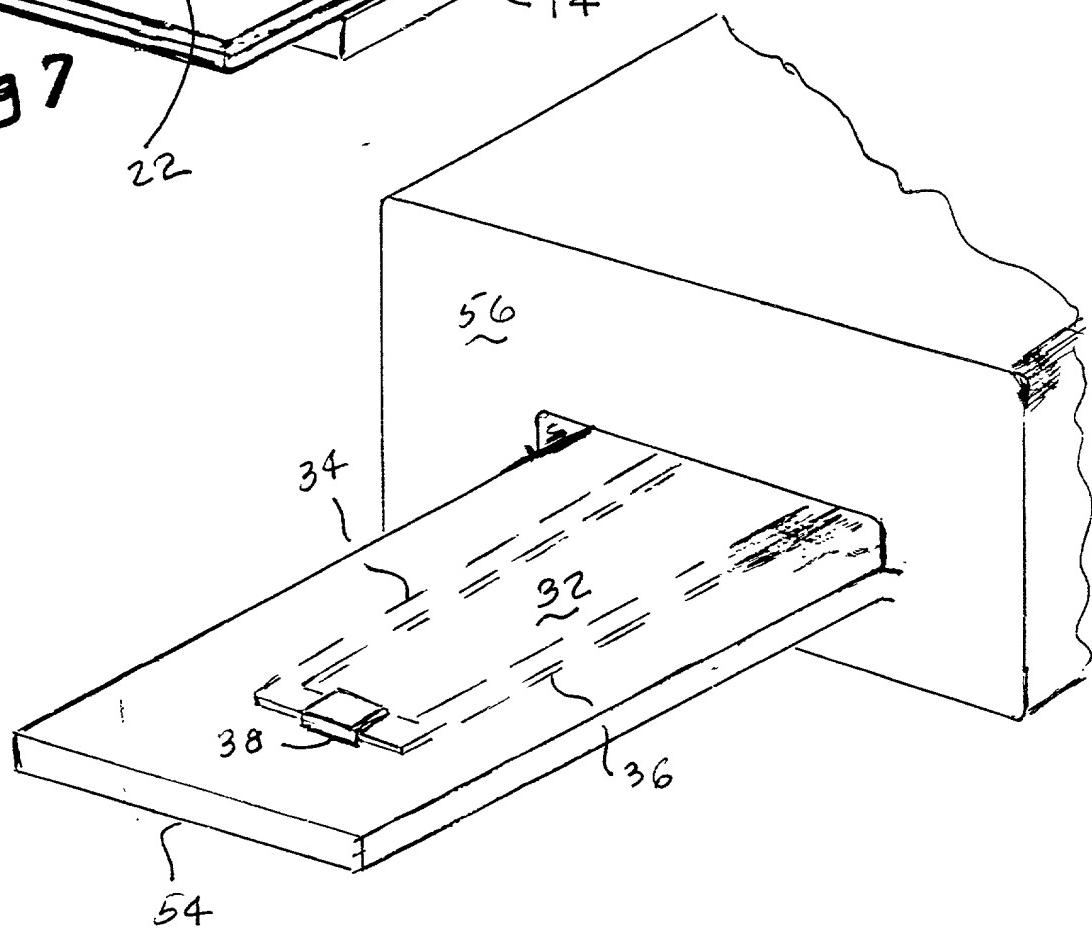
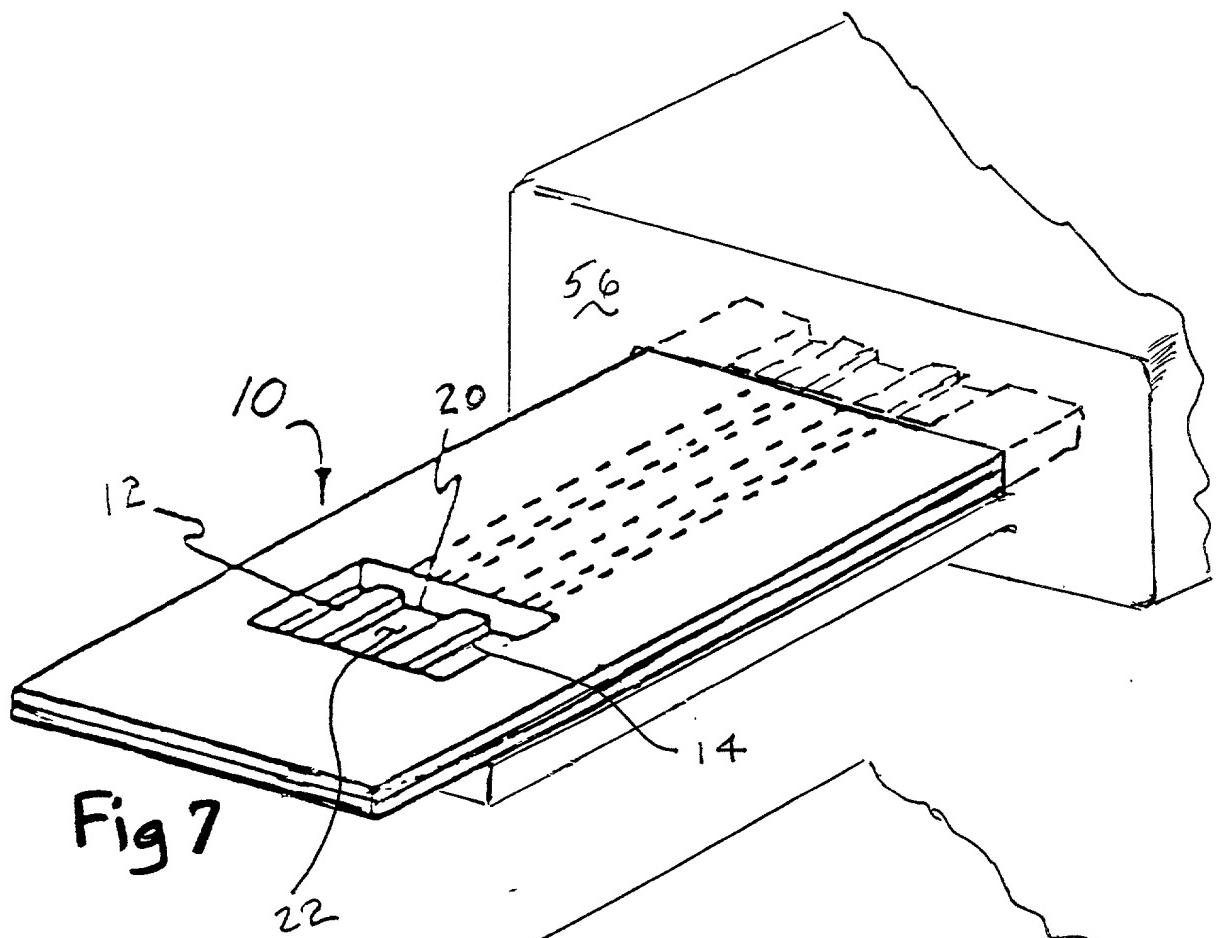


FIG 3





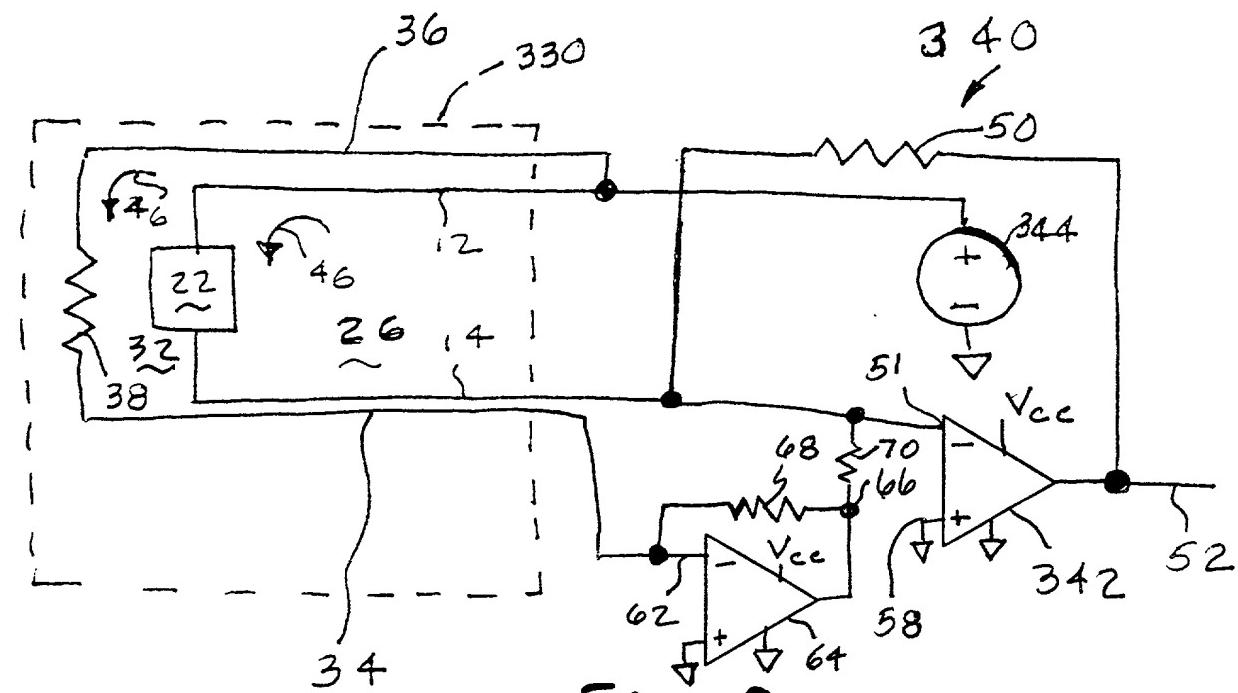


Fig 9

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Maury Zivitz	
Serial No.: To Be Assigned	
Filed: Herewith	
For: BIOSENSOR ELECTROMAGNETIC NOISE CANCELLATION	Docket No. 53009-223482

**COMBINED DECLARATION AND
POWER OF ATTORNEY IN ORIGINAL APPLICATION**

As a below-named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am an original, first and sole inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled BIOSENSOR ELECTROMAGNETIC NOISE CANCELLATION, the specification of which is attached hereto.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims. I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56. I hereby claim foreign priority benefits under Title 35, United States Code, § 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)

<u>Number</u>	<u>Country</u>	<u>Day/Month/Year Filed</u>	<u>Priority Claimed</u>
None	_____	_____	Yes <input type="checkbox"/> No <input type="checkbox"/>
_____	_____	_____	Yes <input type="checkbox"/> No <input type="checkbox"/>

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, § 1.56

which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

Appln. Ser. No.	Filing Date	Status: patented, pending abandoned
<u>None</u>		

I hereby appoint the following attorneys and/or agents to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: Mark W. Binder, Reg. No. 32,642; Felicia J. Boyd, Reg. No. 32,683; Lynn C. Cameron, Reg. No. 44,581; John M. Haurykiewicz, Reg. No. 29,311; Kimberly S. Jordahl, Reg. No. 40,998; David B. Kagan, Reg. No. 33,406; Walter C. Linder, Reg. No. 31,707; Daniel C. Schulte, Reg. No. 40,160; Karl G. Schwappach, Reg. No. 35,786; Gary S. Weinstein, Reg. No. 42,217; and Peter J. Georges, Reg. No. 25,867 (counsel's Washington, D. C. associate); and

Richard T. Knauer, Reg. No. 35,575, Roche Diagnostics/Boehringer, Mannheim Corporation, 9115 Hague Road, P.O. Box 50457, Indianapolis, IN 46250.

Address all correspondence to John M. Haurykiewicz, FAEGRE & BENSON LLP, 2200 Norwest Center, 90 South Seventh Street, Minneapolis, MN 55402-3901, telephone 612/336-3463.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole inventor: Maury Zivitz

Inventor's signature: Maury Zivitz

4/30/00
Date

Residence: 5145 E. 75th Street, Indianapolis, IN 46250

P.O. Address: same as above

Citizenship: United States

M2:20300878.01
(F&B 12/6/99)